PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

JAN 17 2006

PCT

NOTIFICATION CONCERNING TRANSMITTAL OF COPY OF INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (CHAPTER I OF THE PATENT COOPERATION TREATY)
(PCT Rule 44bis.1(c))

To:

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Date of mailing *(day/month/year)*	
05 January 2006 (05.01.2006)	
Applicant's or agent's file reference: WSTR-0020B	IMPORTANT NOTICE

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2004/019603	18 June 2004 (18.06.2004)	18 June 2003 (18.06.2003)

Applicant: THE WISTAR INSTITUTE et al

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Beate Giffo-Schmitt
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Form PCT/IB/326 (January 2004)

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference WSTR-0020B	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/US2004/019603	International filing date *(day/month/year)* 18 June 2004 (18.06.2004)	Priority date *(day/month/year)* 18 June 2003 (18.06.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant THE WISTAR INSTITUTE		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 19 December 2005 (19.12.2005)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Beate Giffo-Schmitt
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Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
JANE MASSEY LICATA
LICATA & TYRRELL PC
66 E. MAIN STREET
MARLTON, NJ 08053

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Applicant's or agent's file reference WSTR-0020B	Date of mailing (*day/month/year*) 18 OCT 2005 **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US04/19603	18 June 2004 (18.06.2004)	18 June 2003 (18.06.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): C12N 15/00, 15/11, 15/09; A61K 48/100 and US Cl.: 536/23.1; 435/320.1; 514/44

Applicant

THE WISTAR INSTITUTE

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☐ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☐ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Ram Shukla Telephone No. (571) 272-0735

Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/19603

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/19603

Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 1-22	YES
	Claims NONE	NO
Inventive step (IS)	Claims NONE	YES
	Claims 1-22	NO
Industrial applicability (IA)	Claims 1-22	YES
	Claims NONE	NO

2. Citations and explanations:

Claims 1-22 lack an inventive step under PCT Article 33(3) as being obvious over YAROSH et al. Human adenovirus type 5 vectors expressing rabies glycoprotein. Vaccine. 1996. vol. 14, no. 13, pages 1257-1264, in view of KANELLOS et al. Naked DNA when co-administered intranasally with heat-labile enterotoxin of Eschericha coli primes effectively for systemic B-an T-cell responses to the encoded antigen. Immunology Letters. 2000. Vol. 74, pages 215-220, and LEITNER et al. Nucleic Acid for the treatment of cancer: Genetic Vaccines and DNA Adjuvants. Current Pharmaceutical Design. 2001, vol. 7 pages 1641-1667.

YAROSH et al. provides guidance on the administration of human adenovirus vectors expressing rabies glycoprotein to mice and skunks (Abstract; pg. 1259, col. 1, materials and methods). Wherein the adenovirus was administered to the mice by i.p. injection and to the skunks by oral vaccination (pg. 1259, col. 1, materials and methods). Further, YAROSH et al. teaches that both routes of administration were able to induce immunization in the host animals (pg. 1261, Table 1; pg. 1262, Table 2).

KANELLOS et al. supplements the guidance provided by YAROSH et al., by teaching a prime-boost strategy of inducing mucosal immunization with plasmid DNA's encoding LacZ and heat labile enterotoxin as an adjuvant (Abstract). Wherein the first dose is administered intranasaly, followed at a later date by i.p. administration of the same plasmid DNA (Abstract, pg. 215, Materials and Methods).

LEITNER et al. supplements the guidance provided by YAROSH et al., by teaching that the removal of neutralizing CpG motifs and the addition of immunostimulatory CpG motifs found on a bacterial backbone enhances the immunogenicity of adenoviral vectors (pg. 1660, col.2, pgph 1).

Based on the guidance provided by YAROSH et al. supplement ed with the teachings of KANELLOS et al. and LEITNER et al. it would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the adenoviral vector by adding CpG motifs so that the vector encoded an adjuvant. Further it would have been obvious to administer the adenovirus vaccine of YAROSH et al. more than once, either orally first then via i.p. administration, or vice versa. Such changes in administration would have been routine in the art at the time of filing.

The practitioner would be motivated to adjust the CpG motifs of the adenoviral vector in order to increase its immunogenicity. Further the practitioner would have been motivated to use a prime boost method of administering the vaccine via both orally and i.p. routes of administration in order to maximize the immune response.

The person of ordinary skill in the art would have a reasonable expectation of success because modifying the adenoviral vector and increasing the number of times it was to be administered would have been routine and minor modifications in the art at the time of filing.

Claims 1-22 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.